REMARKS

Entry of the foregoing, reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

I. Amendments to the Claims

By the foregoing amendments to the claims, claim 12, 15, and 53 have been amended.

In particular, claim 12 has been amended to clarify that the isolated nucleotide sequence encodes a fusion protein comprising the polypeptide of SEQ ID NO: 2 fused in frame with a polypeptide having cytosine deaminase activity. Claim 12 has been further amended to recite that the fusion protein has neither uracil phosphoribosyltransferase nor thymidine kinase activity; this amendment is supported throughout the application as filed, for example at page 1, lines 5-9 of the specification. Furthermore, claim 15 has been amended to correct the dependency, and claim 53 has been amended by replacing the phrase "*polypeptide* of claim 12" with the phrase "*isolated nucleic acid sequence* of claim 12."

In addition, the claim numbering has been revised to correct an error inadvertently introduced in the previous amendment. In particular, the claim numbering has been corrected so there are no longer two claims identified as "claim 54," by re-numbering the last claim as claim 55.

The amendments to the claims have been made without prejudice or disclaimer to any subject matter recited or canceled herein. Applicants reserve the right to file one or more continuation and/or divisional applications directed to any canceled subject matter. No new matter has been added, and entry of the foregoing amendments to the above-identified application are respectfully requested.

II. Response to Claim Rejections Under 35 U.S.C. § 103

A. At pages 4-7 of the Office Action, claims 12-17, 20, 22-29, 39-46, and 54-55 have been rejected under 35 U.S.C. § 103(a) as purportedly unpatentable over Erbs et al. (International Publication No. WO 99/54481) in view of Kern et al. (Gene, 1990, pp. 149-157).

B. At pages 7-8 of the Office Action, claim 21 has been rejected under 35 U.S.C. § 103(a) as purportedly unpatentable over Erbs et al. (International Publication No. WO

99/54481) in view of Kern et al. (Gene, 1990, pp. 149-157), and further in view of Faure et al. (European Publication No. 0206920).

C. At pages 8-10 of the Office Action, claims 18 and 19 have been rejected under 35 U.S.C. § 103(a) as purportedly unpatentable over (International Publication No. WO 99/54481) in view of Kern et al. (Gene, 1990, pp. 149-157), and further in view of Sutter et al. (FEBS Letters, 1995, pp. 9-12) and Carol (Vaccine, 1997, pp. 387-394).

The rejections under 35 U.S.C. § 103 are respectfully traversed.

Initially, Applicants note that to expedite prosecution in the present application, and not to acquiesce to the Examiner's rejections, the claims have been amended as described above. In particular, claim 12 has been amended to recite that the isolated nucleotide sequence encodes a fusion protein comprising the polypeptide of SEQ ID NO: 2 fused in frame with a polypeptide having cytosine deaminase activity, wherein the fusion protein has neither uracil phosphoribosyltransferase nor thymidine kinase activity.

Erbs et al. describes a fusion polypeptide FCU1 (SEQ ID NO: 2) corresponding to the fusion in frame of a polypeptide having uracil phosphoribosyltransferase (UPRTase) activity encoded by the truncated gene FUR1Δ105 (i.e. FUR1 gene whose first 35 N-terminal residues have been deleted; SEQ ID NO: 1) with a polypeptide having cytosine deaminase (CDase) activity encoded by the FCY1 gene. However, in contrast to the present claims, Erbs et al. does not teach or suggest the substitution of an Arg residue at position 183 with a Ser residue in SEQ ID NO: 2, and therefore does not teach or suggest the fusion polypeptide FCU1-8 of the present invention.

Example 5 of Erbs et al. shows results observed with the fusion polypeptide FCU1. Table 3 shows notably that an equivalent UPRTase activity is observed whether the gene is in the fused form (pCI-neoFCU1) or in the unfused form (pCI-neoFUR1Δ105); and that the CDase activity is increased by a factor of 10 when the gene is in the fused form as compared with the unfused FCY1 gene.

Therefore, Erbs et al. demonstrates that the fused polypeptide FCU1 has both UPRTase and CDase activities; and that the fused polypeptide FCU1 also has thymidine kinase (TK) activity. Indeed, as described in Example 6 of Erbs et al., the adenoviral vector is deleted for E1 and E3 regions and contains, in the place of E1, the FCU1 gene.

Kern et al. describes a number of fur1 mutants, including a fur1-7 mutant, a fur1-8 mutant, and a fur1-9 mutant. These mutants are each obtained by one single point mutation (see page 156, left-hand column, §(4) of Kern et al.), resulting in the loss of UPRTase activity

(Table III, page 155 and page 156, first column, §(4) of the reference). Kern et al. also describe a fur1-Δ1 mutant and a fur1-ΔT mutant. The fur1-Δ1 and fur1-ΔT mutants are obtained by deletion of the ClaIb-XbaI segment and the HindIII-XbaI segment, respectively (see page 152, right-hand column, §(c) of Kern et al.), and similar to the fur1-7, fur1-8, and fur1-9 mutants no longer possess UPRTase activity (see Table III, page 155).

However, Kern et al. does not teach or suggest the fusion protein of the present claims. In particular, the reference does not teach or suggest the FUR1Δ105 mutant (i.e. FUR1 whose first 35 N-terminal residues have been deleted) which has moreover maintained UPRTase activity; the substitution of the Arg residue at position 26 with a Ser residue of the FUR1Δ105 mutant in order to lose UPRTase activity; nor the fusion in frame of the FUR1Δ105 mutant including the Arg to Ser substitution, with a polypeptide having CDase activity encoded by the FCY1 gene, where the fusion protein has neither UPRTase nor TK activity. In summary, Kern et al. does not teach or suggest the fusion polypeptide of the present claims having CDase activity but neither UPRTase nor TK activity.

Sutter et al. describes MVA vectors expressing bacteriophage T7 RNA polymerase, Carroll et al. describes MVA vectors expressing ß-galactosidase, and Faure et al. describes poxviruses expressing IFN-γ. None of these three references teach or suggest vectors comprising a nucleotide sequence encoding the FUR1Δ105 polypeptide having UPRTase activity; the FUR1Δ105 polypeptide including the Arg to Ser substitution having no UPRTase activity; or the FUR1Δ105 polypeptide including the Arg to Ser substitution and fused in frame with a polypeptide having CDase activity encoded by the FCY1 gene, where the fusion protein has neither UPRTase nor TK activity. Therefore, Sutter et al., Carroll et al., and Faure et al., taken alone or in the cited combinations, do not teach or suggest a vector comprising a nucleotide sequence encoding the fusion polypeptide of the present claims.

In view of the above, Applicants respectfully request reconsideration and withdrawal of these rejections.

III. Response to Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 12-29, 39-46, and 53-55 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

To expedite prosecution in the present application, and not to acquiesce to the Examiner's rejection, the claims have been amended as set forth above.

Applicants respectfully submit that the claims as amended particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Thus, Applicants respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

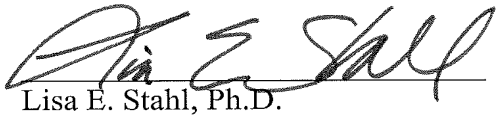
From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

BUCHANAN INGERSOLL & ROONEY PC

Date: June 25, 2009

By: 
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